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Gadolinium-enhanced Magnetic Resonance Angiography, Digital Subtraction Angiography and Duplex of the Iliac Arteries Compared with Intra-arterial Pressure Gradient Measurements

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Purpose: to compare gadolinium-enhanced magnetic resonance angiography (Gd-MRA), digital subtraction angiography (DSA) and duplex of the iliac arteries with intra-arterial pressure gradient measurement as the reference method.

Materials and methods: Gd-MRA, DSA and duplex examinations of the iliac arteries were performed in 30 patients (60 arteries) with lower-limb arterial occlusive disease. In 29 arteries, pressure measurements were made (n=25) or the artery was found to be occluded on catheterisation (n=4).

An aortofemoral peak systolic pressure gradient of 20 mmHg or more was regarded as haemodynamically significant. Stenoses with a diameter reduction of 50% or more on MRA or DSA, or an increase in peak systolic velocity greater than 150% (duplex) were considered significant. MRA examinations were evaluated by means of maximum intensity projections (MRA-MIP) and using source images and curved multiplanar reconstruction (MRA-MPR).

Results: the sensitivity (specificity) for a significant iliac artery stenosis were 81% (75%) for MRA-MIP, 76% (75%) for MRA-MPR, 86% (88%) for DSA, and 72% (88%) for duplex.

Conclusion: with intra-arterial pressure measurements as the reference method, similar results were achieved with Gd-MRA, DSA and duplex concerning the detection of haemodynamically significant iliac artery stenoses. The use of source images and multiplanar reconstructions resulted in higher accuracy for the detection of occlusions.

Key Words: MRA; Gadolinium; DSA; Duplex; Pressure measurement; Iliac artery.

Introduction

Accurate evaluation of the location and haemodynamic severity of the lesion is the most important task prior to surgical or endovascular intervention for lower-limb occlusive arterial disease. Conventional angiography, commonly performed as intra-arterial digital subtraction angiography (DSA), is generally accepted as the “gold standard”. Duplex ultrasonography and magnetic resonance angiography (MRA) have emerged as possible non-invasive alternatives in recent years. Gadolinium-enhanced MRA (Gd-MRA) of the aortoiliac arteries has recently been shown to correlate well with DSA in the detection and grading of iliac artery atherosclerotic lesions.^{1–4} Duplex scanning of the iliac arteries has also shown good correlation with DSA.⁵ The limitations of conventional

angiography with regard to the detection of subcritical stenosis are well known. For example, in one study angiography failed to detect 25% of the haemodynamically significant stenoses in the aortoiliac tract.⁵ For this reason, intra-arterial pressure-gradient measurement across an iliac stenosis is considered by many authors to be the “gold standard”.^{5–7} In one study using pressure gradient as reference method, MRA without contrast enhancement (time-of-flight technique) was found to have a sensitivity of 85% and a specificity of 80% regarding haemodynamically significant iliac artery stenoses.⁸ To the best of our knowledge there have been no previous studies in which Gd-MRA has been compared with intra-arterial pressure measurements in the evaluation of the iliac arteries. The aims of the present study were:

- (i) to compare the findings of Gd-MRA, DSA, and duplex scanning with those of intra-arterial pressure measurements, as the reference method, and
- (ii) to compare maximum intensity projections (MIPs) and with the use of source images and multiplanar

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reconstructions (MPRs) in the assessment of aorto-iliac cardiac disease.

Materials and Methods

Material

Patients with clinical signs of iliac artery occlusive disease were eligible for inclusion in the present study if a routine duplex examination of the pelvis arteries showed at least one iliac artery stenosis on either side, or if the examination was inconclusive. From October 1996 to April 1998, 30 non-consecutive patients were included in the study. Of these, 28 had symptomatic chronic lower limb ischaemia and two were asymptomatic being examined in the follow-up after previous vascular surgery. Twenty patients had claudication, and eight patients had rest pain and/or ulcer or gangrene. All patients were examined with duplex, Gd-MRA, and DSA, according to a prospective protocol. The patients' ages ranged from 49 to 83 years (median 71.5 years); 17 were males and 13 were females. The time interval between the MRA and DSA examinations was 0–15 days (median 1.5 days). Intra-arterial pressure measurements in the lower abdominal aorta and the common femoral artery were performed during DSA in 25 patients (27 iliac arteries).

Gadolinium-enhanced MRA

All patients were examined with a 1.5-T scanner (Philips Gyroscan ACS NT, Best, The Netherlands) with a gradient of 10 mT/m and a slew rate of 0.6 mT/m/ms. A quadrature body coil was used.

After an initial survey scan to define the volume of interest, a test dose scan was performed with injection of 2 ml of a gadolinium contrast agent (Omniscan 0.5 mmol/l, Nycomed Amersham Imaging, Oslo, Norway) at 1 ml/s, followed by a saline flush of 20 ml at a rate of 1 ml/s. Contrast agent injections were made through a cannula inserted in a forearm vein, connected to a power injector (Spectris, Medrad, Indianola, PA, U.S.A.). Using a two-dimensional gradient echo (2DGRE) sequence (repetition time [TR]/echo time [TE]/flip angle [FA]: 12 ms/3.3 ms/50°), an axial slice over the lower abdominal aorta was repeated every second. The arrival time of the test bolus was determined by visual examination of the acquired dynamic phases. To minimise inflow effects, an 80 mm thick presaturation slab was placed superior to the slice.

During the main scan the contrast agent was administered at a rate of 1 ml/s, to a total volume of 40 ml (30 ml in eight patients). On the basis of the test dose scan, the scan delay was chosen so that the bolus arrived in the upper part of the examination volume at the start time of the scan. Based on a multiple two-dimensional (M2D) inflow planning scan, slices were placed in the coronal plane or a plane close to this, care being taken to include the iliac arteries. Imaging was made with a three-dimensional (3D) radio frequency (RF)-spoiled GRE sequence during free breathing, with TR/TF/FA of 12–16 ms/5–5.7 ms/50°, fixed for the last 14 patients to 14 ms/5 ms/50°, giving a median examination time of 1:07 min (range 1:01–1:30). Nineteen 4-mm coronal slices were obtained which, with zero-filling, were reconstructed to 38 slices of 2 mm. The field of view (FOV) was 360 mm × 360 mm with a matrix size of 261 × 512 (292 × 512 in four patients), resulting in a resolution of 1.4 (1.2) × 0.70 × 4 mm. Partial echo was chosen in order to minimise the echo time. First order flow compensation was used. No fat saturation or subtraction was made. Linear k-space order was used, so that the central part of the k-space was acquired in the middle of the acquisition interval.

For evaluation purposes, maximum intensity projections were created on the operator's console using standard software. Eighteen MIPs covering 180 degrees around the longitudinal axis were made. Four MIPs were selected for evaluation purposes: two oblique, one frontal, and one magnified view in the projection best showing the relevant pathology. In addition, curved multiplanar reconstructions were made on a workstation (Easyvision, Philips, Best, The Netherlands).

DSA

Conventional angiography was performed with the digital subtraction technique on a single-planar X-ray unit (Philips DVI-S, Best, The Netherlands). The femoral artery was punctured in the groin on the symptomatic side, with insertion of a 6F introducer (Radifocus 100 mm, Terumo Corporation, Tokyo, Japan). Through this a 35-cm 5F straight end-hole catheter (Cook, Bloomington, IN, U.S.A.) was inserted until its tip was situated in the lower abdominal aorta. Through the introducer 5000 IU heparin were administered.

Images of the pelvic arteries including the lower abdominal aorta were obtained in frontal and two 20 degrees oblique projections (in one patient, only one

projection). For each series 20–30 ml of a non-ionic low-osmolar contrast agent (Omnipaque, 180 mg/ml, Nycomed Amersham Imaging, Oslo, Norway) was injected at a rate of 10–15 ml/s with a power injector (Medrad, Indianola, PA, U.S.A.). In order to minimise bowel peristalsis, 20 mg of a peripheral anticholinergic drug (Buscopan, Boehringer Ingelheim, Ingelheim, Germany) was administered intravenously prior to the imaging.

Arterial pressure measurements

Pressure measurements were made in conjunction with the DSA examinations, before administration of contrast agent. The 5F catheter (with its tip in the lower aorta) and 6F introducer (with its tip in the common femoral artery) were connected to pressure transducers via saline-filled lines of equal length. Simultaneous systolic pressure recordings from the two sites made it possible to calculate the systolic pressure gradient over the iliac segment. If this gradient was less than 20 mmHg, the measurement was repeated 45 s after this injection of 60 mg papaverine into the lower abdominal aorta through the 5F catheter.

Duplex examination

Duplex scanning was performed with an Acuson 128 XP model with a 5-MHz linear array probe (Acuson, Mountainview, CA, U.S.A.). The examiner was unaware of the results of the MR angiography and DSA results. The distal aorta, and the common (CIA) and external iliac arteries (EIA) were searched for colour changes suggestive of an arterial lesion. Peak systolic velocities (PSVs) from these areas were compared with those from the normal segment immediately proximal to the stenosis. In brief, a focal increase of PSV greater than 150% of that in the normal segment was considered as indicative of a 50% or greater stenosis when the Doppler was ≤ 60 degrees. Occlusions were diagnosed when no flow was detected despite attempts to maximise sensitivity to slow arterial flow by increasing Doppler gain and decreasing the colour scale.

Evaluation

The MRA, DSA, and duplex examinations were interpreted by three different observers, blinded to the findings with the other modalities. In order to identify

the corresponding lesion or normal section of the vessel, the arteries were divided into five segments: the lower abdominal aorta, right and left CIA and EIA. Each segment was graded, according to the most pronounced lesion, into three grades:

- 1 = normal or mildly stenosed (0–49% diameter reduction),
- 2 = severely stenosed (50–99% diameter reduction), or
- 3 = occluded.

The nearest normally appearing vessel segment was used as a reference for calculating the diameter reduction at the site of the stenosis. When the vessel was graded as being on the borderline between groups, the higher value was used for analysis. This was the case in the DSA protocol for one common iliac artery, graded as 1–2. No borderline gradings were assigned to the MRA, or duplex examinations. In 30 patients, conclusive DSA investigations were made in 148/150 vessel segments. One DSA examination covered only one side of the iliac territory, resulting in three examined segments. MRA examinations were evaluated by using selected MIPs (MRA-MIP), and by using source images as well as curved MPRs in freely chosen planes (MRA-MPR).

In 30 patients (148 segments) with DSA evaluations there were assessable MRA-MIP examinations in 145/148 vessel segments and assessable MRA-MPR examinations in 140/148 vessel segments. Three EIAs were excluded because: vessel partially outside the FOV (one), signal loss due to ipsilateral metal hip replacement (one), and signal loss due to vascular stents (one). The MRA-MPR evaluation could not be made in one patient because of lost raw data. The corresponding number of vessel segments for duplex scanning was 132/148. There were inconclusive scans in two aortas and four iliac segments. In five cases unilateral duplex scanning of the iliac artery was performed.

Pressure gradient measurements were performed in 25 patients, bilaterally in two cases. The measurements were regarded as inconclusive in two patients. In one patient the distal pressure recording was considered irrelevant, as the distal measurement was made from within a tight stenosis, and in another because measurements after papaverine injection showed higher pressures distal to a stenosis. This was believed to be the result of diminishing vasodilatation. In addition to the 25 conclusive pressure gradient measurements, there were four cases in which an occlusion in the common or external artery was found during ipsilateral catheterisation. This was considered to be equivalent to the finding of a haemodynamically significant pressure gradient, and these cases were added to the

group of segments with pressure gradient measurements, resulting in 29 aortoiliac segments. Assessable MRA and DSA examinations were obtained on all 29 sides with conclusive pressure measurements. Conclusive duplex results were obtained on 26/29 sides.

Statistical analysis

In order to calculate the sensitivity and specificity of the different modalities, a dichotomous classification was used. Negative findings consisted of vessels that were normal or mildly stenosed. Vessels with severe stenoses (50–99% diameter reduction) or occlusions were classified as positive findings.

In the group with systolic pressure recordings (29 aortoiliac segments), the sensitivity, specificity, and positive- and negative-predictive value for the finding of a haemodynamically significant lesion in the common or external iliac arteries were calculated for MRA with MIP, MRA with MPR, DSA, and duplex, with systolic pressure gradient measurements as the method of reference.

For the whole series (148 segments), a comparison was made between MRA-MIP, MRA-MPR, and duplex, with DSA as the method of reference. The agreement between methods according to the 3-grade scale was evaluated with the weighted kappa coefficient (κ_w).⁹ The sensitivity, specificity, and positive- and negative-predictive values regarding stenoses with diameter reduction of $\geq 50\%$ were calculated for the vessel segments.

The statistical significance of differences in sensitivity and specificity was tested with a logistic regression model predicting the diagnostic outcome from patient identity, vessel segment and method chosen, in the appropriate subpopulation. These calculations were carried out in JMP 3.1 (SAS Institute, Inc., Cary, NC, U.S.A.). A p -value of 0.05 was chosen as the threshold for statistical significance.

Results

MRA, DSA, and duplex compared with pressure gradient recordings

The results of the MRA, DSA, and duplex examinations, with pressure-gradient measurements as

Table 1. Number of significant stenoses with pressure gradient as reference.

| | Pressure gradient | | |
|---------|-------------------|-----|-------|
| | Neg | Pos | Total |
| MRA-MIP | | | |
| Neg | 6 | 4 | 10 |
| Pos | 2 | 17 | 19 |
| Total | 8 | 21 | 29 |
| MRA-MPR | | | |
| Neg | 6 | 5 | 11 |
| Pos | 2 | 16 | 18 |
| Total | 8 | 21 | 29 |
| DSA | | | |
| Neg | 7 | 3 | 10 |
| Pos | 1 | 18 | 19 |
| Total | 8 | 21 | 29 |
| Duplex | | | |
| Neg | 7 | 5 | 12 |
| Pos | 1 | 13 | 14 |
| Total | 8 | 18 | 26 |

the reference method, are summarised in Table 1. Pressure drops of ≥ 20 mmHg or occlusions verified by catheterisation were found in 21/29 arteries (72%). The sensitivity, specificity, and positive- and negative-predictive values for the methods are listed in Table 2. DSA had the highest values for all these parameters (along with duplex for specificity). There were no statistically significant differences in sensitivity or specificity between the methods ($p > 0.05$).

MRA and duplex compared with DSA

The gradings of each segment with MRA and duplex compared with DSA are shown in Table 3. Both MRA methods had a higher sensitivity than duplex for the detection of lesions with minimum 50% diameter narrowing, and this difference was statistically significant ($p < 0.01$). There was no significant difference regarding the sensitivity between the two MRA methods ($p = 0.23$). The specificity was higher with MRA-MPR than with MRA-MIP, and this difference was almost statistically significant ($p = 0.053$).

MRA-MPR compared favourably to MRA-MIP concerning the assessment of vessel patency (Fig. 1). MRA-MIP showed occlusions in five segments where patent vessels were seen with DSA, while with MRA-MPR there was only one segment that was falsely graded as occluded. Six segments were graded as occluded with duplex, where DSA showed no occlusion. The weighted kappa coefficients suggest a better agreement between the MRA evaluations and DSA than between duplex and DSA.

Table 2. Sensitivity, specificity, positive-predictive value, and negative-predictive value [95% confidence interval] for MRA, DSA, and duplex regarding significant iliac artery stenoses, with pressure gradients as reference.

| | Sensitivity (%) | Specificity (%) | Positive predictive value (%) | Negative predictive value (%) |
|---------|-----------------|-----------------|-------------------------------|-------------------------------|
| MRA-MIP | 81 [64–98] | 75 [45–100] | 89 [76–100] | 60 [30–90] |
| MRA-MPR | 76 [58–94] | 75 [45–100] | 89 [74–100] | 55 [25–84] |
| DSA | 86 [71–100] | 88 [65–100] | 95 [85–100] | 70 [42–98] |
| Duplex | 72 [47–90] | 88 [47–100] | 93 [66–100] | 58 [28–85] |

Table 3. Sensitivity (Sens.), specificity (Spec.), positive-predictive value (PPV), negative-predictive value (NPV), and weighted kappa value (κ), with 95% confidence intervals for MRA, and duplex regarding significant iliac artery stenoses, with DSA as reference.

| | Sens. (%) | Spec. (%) | PPV (%) | NPV (%) | κ |
|---------|------------|------------|------------|-------------|------------------|
| MRA-MIP | 91 [82–99] | 79 [71–87] | 66 [54–78] | 95 [91–100] | 0.67 [0.50–0.85] |
| MRA-MPR | 81 [69–92] | 89 [83–95] | 76 [63–88] | 92 [86–97] | 0.72 [0.52–0.92] |
| Duplex | 63 [48–79] | 85 [78–92] | 63 [48–79] | 85 [78–92] | 0.43 [0.21–0.64] |

Discussion

With pressure-gradient measurements as the method of reference, there were no statistically significant differences between MRA, DSA and duplex regarding the detection of haemodynamically significant iliac stenoses. Some overestimation of stenoses seems to have occurred with the MRA methods, as reflected in a somewhat lower specificity (75%) compared with DSA (88%) and duplex (88%). Source images and multiplanar reconstructions were valuable for the assessment of vessel patency, but in this study did not improve the MRA results compared with those of MIPs concerning the detection of haemodynamically significant stenoses.

In the present study, with DSA as the reference method, the sensitivities of Gd-MRA with MIP and MPR regarding lesions with a diameter reduction of at least 50% were 91% and 81% respectively. Other investigators have reported somewhat higher values of 93–100%.^{1–4} The corresponding specificities in three of the studies were 89–100%^{1,3,4} and in the fourth (two observers) 62–87%.² Two of these studies^{3,4} were carried out with higher performance gradients, enabling the use of a shorter echo time as well as a higher injection rate because of the shorter acquisition time, both of which result in an improved contrast-to-noise ratio. These discrepancies in the MRA techniques employed can at least partly explain the superiority of the results over ours.

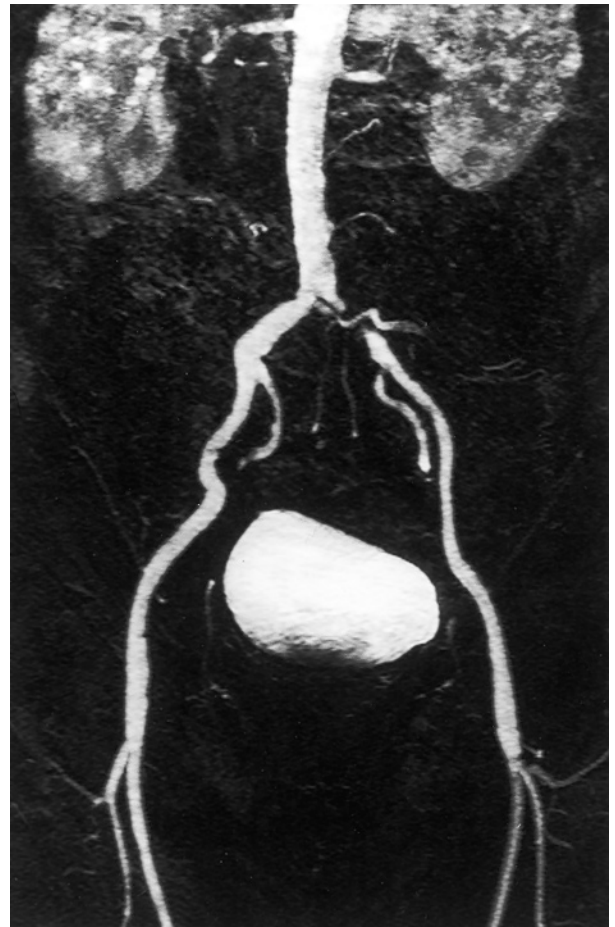
Intra-arterial pressure measurement has gained acceptance as a more reliable reference method than DSA. It has been shown that an arterial stenosis does not reduce the blood flow until a certain degree of luminal narrowing is reached.^{6,7} This “critical stenosis” is dependent on the normal calibre and blood flow velocity of the vessel in question.⁷ In the iliac arteries,

a diameter reduction of about 50% has been found to represent a critical stenosis.⁷ Above this level, any incremental narrowing results in a profound decrease in blood flow. Borderline lesions are thus difficult to evaluate with morphological methods, since subtle differences in vessel calibre can imply large differences in flow. This is the reason why pressure-gradient recordings are required before a decision on surgical or endovascular therapy is made. In addition, it has been shown that tandem subcritical lesions can cause significant pressure drops.¹⁰ This stenosis pattern is difficult to evaluate with morphological methods such as DSA, which is often used as a reference method.^{2–5} For these reasons we chose pressure recordings as the reference method in this study. Furthermore, the three-dimensional nature of a MRA examination, with the choice of arbitrary projections and MPRs is an advantage over DSA, which makes DSA less well suited as a reference method.

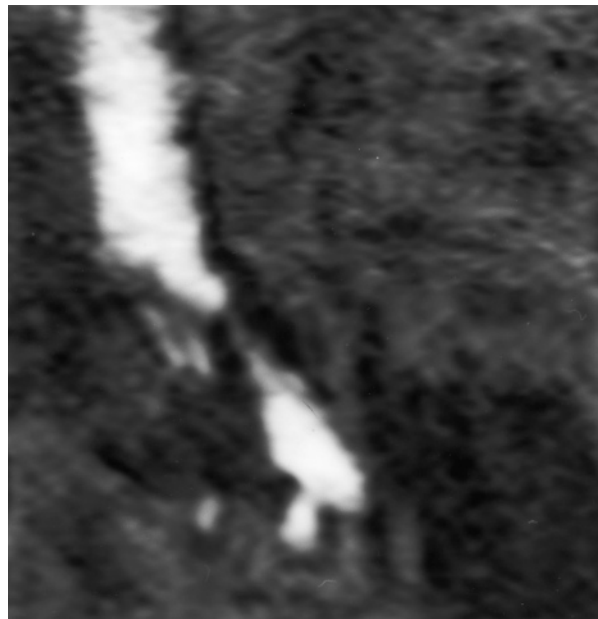
Different absolute or relative values for mean or systolic pressure gradients, with or without pharmacological vasodilatation, have been proposed as thresholds for a haemodynamically significant iliac artery stenosis. In line with a previous report,¹¹ we chose to use a systolic pressure gradient of 20 mmHg after peripheral vasodilatation with papaverine to represent the lower limit for a significant stenosis. Some technical aspects are important for obtaining valid pressure recordings. The proximal and distal pressure recordings should preferably be obtained simultaneously. Otherwise the pressure gradient will be affected by normal fluctuations in the pressure level and be more uncertain. This is especially important after peripheral vasodilatation, when larger temporal pressure variations occur. Simultaneous pressure recordings can be obtained in two ways. Catheters can be positioned from both sides, one ipsilateral to the



(a)



(b)



(c)

Fig. 1. A left-sided common iliac artery is seen to be occluded on (a) DSA and (b) maximum intensity projection of MRA. A curved multiplanar reformat of the MRA (c) shows a severely stenosed, but patent, vessel.

measured side into the femoral artery, and one from the contralateral side into the lower aorta. This method has the disadvantage of requiring bilateral groin punctures. The coaxial system that was used requires only unilateral puncture. The drawback of this technique is that the inner catheter has to be placed across the pressure-measured segment, which might introduce an artefactual pressure gradient, depending on the vessel calibre as well as on the catheter dimension.¹²⁻¹⁵ Given the normal size of the iliac arteries and the diameter (1.6 mm) of the catheter used, our pressure recordings were probably not significantly altered. Care must be taken not to make the pressure measurement within a narrowed segment, where the measurement may be influenced by a local flow disturbance. Discrepancies between pressure measurements and the findings in morphological studies can occur in low-flow situations. Since the pressure drop is proportional to the blood flow velocity,⁶ a lesion that is apparently significant on DSA or MRA might not cause a significant pressure drop if the peripheral resistance is high or the cardiac output low. The technique used here did not permit localisation of a significant lesion within the aortoiliac segment. For this purpose a pull-back technique can be employed.¹⁴

In addition to the advantage of not using ionising radiation, MRA is non-invasive and does not require potentially nephrotoxic contrast agents. The latter is of special interest in this particular category of patients, since they include a substantial proportion with impaired renal function.¹⁶ If desired, a concomitant evaluation of the renal arteries can be accomplished with modern MR gradient systems permitting shorter scans during breath-hold.^{3,4} In most patients with suspected aortoiliac lesions there is also a need for an assessment of the infrainguinal arterial tree. This can be achieved today with multi-station examinations encompassing the arteries from the aorta to the ankle.^{17,18} The longer acquisition time with MRA compared to DSA may be of benefit for the simultaneous visualisation of in- and outflow vessels.

The use of multiplanar reconstructions did not improve the MRA results compared with those obtained with maximum intensity projections alone, except for the assessment of vessel patency. The three-dimensional nature of a MRA examination might, however, be further utilised. With use of multiplanar reconstructions perpendicular to the vessel, calculations of the area reduction can be made, which might improve the accuracy compared with the generally performed assessment of the diameter reduction, especially for eccentric lesions. There is a possibility that this evaluation can be computerised.

An assessment of the aortoiliac inflow tract is important in patients with symptoms of lower-limb arterial occlusive disease. The results of this study show that this can be achieved non-invasively by means of MRA, with results similar to those of DSA. Duplex also proved useful for the aortoiliac evaluation, but has the disadvantage of being operator-dependent.

Intra-arterial pressure gradient measurement remains an important tool, since neither MRA, DSA, nor duplex could identify all of the lesions proven to be haemodynamically significant. A reliable MR method for estimation of the intravascular pressures would, together with an MRA examination, allow a complete, non-invasive, arterial evaluation. Such an estimation will probably include measurements of blood flow velocity, which is more closely related to the pathophysiological effect of the stenosis.

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